REMARKS

Claims 1, 2, 9-15, 17, and 19-21 were pending at the time of the Office Action. Claims 10, 12, 13, 20, and 21 stand withdrawn as drawn to non-elected subject matter. Claims 1, 2, 9, 11, 14, 15, 17, and 19 stand rejected under 35 U.S.C. § 102(b). Claims 9, 11, and 19 stand objected to under 37 C.F.R. § 1.75(c). Claim 14 stands rejected under 35 U.S.C. § 101. Applicants address each of these rejections and objections below.

Amendments to the Claims

Claim 1, 14, and 15 have been amended to remove the term "CD8+." Claim 1 has been further amended to include a step of detecting and/or purifying activated T cells transduced with the gene. Support for this amendment is found, e.g., on page 32, lines 6-24, and pages 34, line 6, to page 38, line 3, of the English-language specification as filed. Claim 11 has been amended to require that the step of stimulating T cells with an antigen occurs prior to the contacting step, thereby obtaining the activated T cells. Support for this amendment is found, e.g., on page 3, lines 19-22, of the English-language specification as filed. Claim 14 has been amended to feature isolated, purified, and activated T cells transduced with a gene carried by a paramyxovirus vector. Support for this amendment is found, e.g., on page 6, lines 1-33, and on page 28, lines 2-3, of the English-language specification as filed. Claim 15 has been amended to require that the contacting step includes contacting the paramyxovirus vector carrying the gene with a

mixture of naive T cells and activated T cells. Support for this amendment is found, e.g., on page 4, lines 27-33, of the English-language specification as filed. Claims 17 and 19-21 have been cancelled.

New claims 22-29 have been added. Claim 22, which depends from claim 1, features the step of purifying activated T cells transduced with the gene. Support for this claim is found, e.g., on page 32, lines 6-24, and page 34, line 6, to page 38, line 3, of the English-language specification as filed. Claims 23-29 correspond to claims 1, 2, 9, 11, 15, 22, and 14, respectively, and further feature activated CD8+ T cells. Support for this feature is found, e.g., on page 32, lines 18-20, and page 34, lines 6-16, of the English-language specification as filed.

The present amendments were made to expedite prosecution, and applicants reserve the right to pursue any cancelled subject matter in this or in a continuing application. No new matter has been added.

Rejection Under 35 U.S.C. § 102(b)

Claims 1, 2, 9, 11, 14, 15, 17, and 19 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Yu et al. (Genes to Cells, 2:457-466, 1997; "Yu"), as evidenced by Mauri-Hellweg et al. (J. Immunol. 155:462-472, 1995; "Mauri-Hellweg"). The Office states (page 3):

> [T]he PBMCs of Yu et al. must necessarily comprise activated $CD8^+$-T cells...the method of Yu et al. must necessarily result in enhanced transfection efficiency since it involves activation of $CD8^+$-T cells before contacting them

with the Sendai virus vector.

Applicants disagree. Yu does not teach T cells transduced with a paramyxovirus vector. As applicants noted in the reply filed on June 18, 2007 (page 7), the assertion that the PBMC cells of Yu inherently include activated CD8+ T cells is not based on any evidence of record and constitutes speculation. The Office's citation of Mauri-Hellweg does not provide any evidence that the PBMC cells of Yu inherently include activated CD8+ T cells. Indeed, Mauri-Hellweg relates to activation of drug-specific CD4+ and CD8+ T cells in individuals allergic to particular drugs, and states (page 468, left column):

> [H]ealthy nonallergic donors had no activated CD4+ or CD8+ T cells in the circulation.

Nevertheless, to expedite prosecution, claim 1 has been amended to include a step of detecting and/or purifying activated T cells transduced with the gene and to remove the term "CD8+." In addition, claim 14 has been amended to feature isolated, purified, and activated T cells. Neither Yu nor Mauri-Hellweg, taken alone or in combination, teach or suggest all the elements of claims 1 or 14, as amended.

Applicants further note that the present invention demonstrates that the gene transduction efficiency of naive T cells with a paramyxovirus vector is low, while the activation of T cells significantly enhances the gene transduction efficiency with a paramyxovirus vector. The cited art neither teaches nor suggests this effect of the activation of T cells.

Regarding Yu's teaching of MT4 and Molt 4 cell lines, applicants submit that

these are not T cell lines but rather established immortalized cell lines originally derived from CD4+ T leukemic cells. Established immortalized cell lines are not T cells. In the reply filed on October 16, 2006, applicants stated (page 9):

> MT4 is an acute lymphoblastic leukemia cell line transformed with human T-cell leukemia virus type 1, as shown in Exhibit 1 (data sheet from the National Institutes of Health AIDS Research & Reference Reagent Program). Similarly, Molt 4 is a leukemic cell line derived from a patient suffering from an acute lymphoblastic leukemia in relapse, as shown in Exhibit 2 (an additional National Institutes of Health data sheet). These cells are distinct from the T cells featured in the claims as presently amended.

Applicants also noted (page 10) that Thenet et al. (J. Cell. Physiol. 150: 158-167, 1992) describe the establishment of an immortalized rabbit articular chondrocyte cell line and state (abstract):

> [T]he resulting cell lines displayed an apparently irreversibly dedifferentiated phenotype.

Likewise, Jat et al. (Proc. Natl. Acad. Sci. U.S.A. 88: 5096-5100, 1991) describe the derivation of conditionally immortal cell lines from a transgenic mouse and state (page 5096, right column, lines 4-6):

> An additional problem associated with the introduction of immortalizing genes into cells is that these genes can alter normal cellular physiology...

These references show that established immortalized cell lines have distinct cellular physiology from original cells, and their phenotypes are irreversible. Accordingly, MT4 and Molt 4, as disclosed in Yu, are no longer T cells.

Furthermore, T cells differ from MT4 and Molt 4 in the following respects:

(i) MT4 and Molt 4 are established immortalized cell lines derived from a patient suffering from leukemia and having the ability to divide indefinitely. There is no possibility of using MT4 and Molt 4 for therapy.

(ii) While MT4 and Molt 4 can theoretically propagate indefinitely, the lifetime of T cells collected from a living body is only several weeks.

(iii) MT4 and Molt 4 lack the intrinsic ability of T cells to (a) propagate in an antigen-specific (MHC class I-restricted) manner, (b) recognize the antigen-expressing cells and migrate and locally accumulate to the target cells, and (c) kill the target cells in an antigen-specific manner.

Thus, MT4 and Molt 4 cells are not T cells.

In view of the above arguments and amendments, the rejection of claims 1, 2, 9, 11, 14, 15, 17, and 19 under 35 U.S.C. § 102(b) should be withdrawn. New claims 22-29 depend from the preceding claims and are accordingly free of this basis of rejection as well.

Objection Under 37 C.F.R. § 1.75(c)

Claim 11 stands objected to under 37 C.F.R. § 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. The Office states (page 4):

> Claim 11 recites a method comprising the step of stimulating the T-cells with an antigen. However, claim 9, from which claim 11 depends, already recites that the activated T-cells are antigen-activated.

Claim 11, as amended, requires that the recited step of stimulating T cells with an antigen occurs prior to the contacting step recited in claim 9, thereby obtaining the activated T cells. That is to say, the stimulating step of claim 11, as amended, produces the antigen-activated T cells recited in claim 9. Claim 11, as amended, is unambiguous, and therefore the objection to claim 11 under 37 C.F.R. § 1.75(c) should be withdrawn.

In addition, claims 9, 11, and 19 stand objected to under 37 C.F.R. § 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. The Office states (page 5):

> Claims 1 and 17 recited $CD8^+$ T-cells, whereas their dependent claims 9, 11, and 9 [sic] recite the broader limitation of T cells.

Claim 1, as amended, does not recite CD8+ T cells. Claims 17 and 19 have been cancelled. Thus, the objection to claims 9, 11, and 19 under 37 C.F.R. § 1.75(c) should be withdrawn.

Rejection Under 35 U.S.C. § 101

Claim 14 stands rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. The Office notes (page 5) that amending the claim to recite "isolated" would obviate the rejection. Claim 14 has been amended as the Office suggested, and therefore the rejection under 35 U.S.C. § 101 may now be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. Enclosed is a petition to extend the period for replying to the Office Action for two months, to and including February 7, 2008.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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